

SPL Working Group SPLIMAGE Workshop

(held July 26, 2012 on the campus of the National Library of Medicine)

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Some Definitions of Projects/Terms:

Acronym	Expansion or definition
C3PI	Computational Photography Project for Pill Identification <ul style="list-style-type: none">• Use of digital macrophotography to develop inventory of digital images of solid oral dose formulations
FDA	Food and Drug Administration
HPCC	High Performance Computing and Communications [a group within the National Library of Medicine]
NLM	National Library of Medicine
PILLBOX	Information product of NLM Specialized Information Systems. <ul style="list-style-type: none">• SPLIMAGE files are an integral part of this product, more information is included in Federal Register notice here
SIS	Specialized Information Services [a group within the National Library of Medicine]
SODF	Solid Oral Dose Formulation (capsule, tablet, etc.)
SPLIMAGE	An image of a solid oral dose formulation taken according to the v3.0.2 SPLIMAGE specification

Minutes, Actions, and Questions for Further Discussion

Introductions and Overview of Activities

On May 23, 2011, NLM posted a Federal Register Notice (Vol. 76, No. 99, FR Doc. 2011–12629, <http://www.gpo.gov/fdsys/pkg/FR-2011-05-23/html/2011-12629.htm>), seeking sources of medications to develop the photographic techniques to capture this information. In June 2012, the first results of an ongoing study of digital photographs of voluntarily submitted medications by pharmaceutical manufacturers have been released.

The SPL Working Group organized a one-day SPLIMAGE workshop to discuss these results and what might be happening in the future. Attendees included representatives from companies (sponsors) that provided samples in response to the May 2011 Federal Register notice, NLM representatives involved with the SPLIMAGE image production and dissemination, FDA representation from those involved with SPL and the SPLIMAGE discussions, and potential downstream users of the SPLIMAGEs.

At several points in the day, we acknowledged (through applause) the contributions of the many individuals and groups in the process. The contributions of the SIS (Specialized Information Services) and HPCC (High Performance Computing and Communications) groups from NLM, the sample provision and patience of the sponsors providing samples, the partnership of the FDA and NLM for both DailyMed and this SPLIMAGE initiative, the support of the SPL Working Group,

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and the input from the downstream users (e.g., compendium producers) were all necessary for this effort to get to the point of a single image of a solid oral dose formulation product appearing in an SPL on DailyMed. [Dr. Donald A.B. Lindberg](#), Director of the National Library of Medicine stopped by to congratulate everyone on the efforts to move this initiative forward and stayed for a live demonstration of the imaging technology that is being used in this SPLIMAGE program.

The notes, actions and questions arising from this workshop will be available from the SPL Working Group WIKI, and disseminated through e-mail and other distribution methods. Additionally, copies of slide presentations from the workshop will also be made available.

NLM Orientation – the people & activities behind the recent set of images [\[Slideset available\]](#)

Associated SLIDASET provides details on the organization structure within NLM for the groups

The SPLIMAGE activities were and are part of an established collaboration with FDA SPL. The photos were taken by the computer vision research project of NLM LHC/HPCC “Computational Photography Project for Pill Identification (C3PI) Program”, in part to establish digital content.

The driving motivation for the projects and this workshop is consumer safety. The effectiveness of the SPLIMAGE relies, in part, on a deep understanding of digital macrophotography to make best use of light, backgrounds, and the natural variability of the solid oral dose forms.

To date:

- SPLIMAGE specification (produced by NLM) posted in March 2012 [SPLIMAGE specification](#) (v3.0.2)
- As of July 26, 2012, NLM photographed 144 Oral Solid Dosage Forms received via the information provided in the FR notice [here](#). These images have been provided to the companies that submitted the samples.
 - Of those, 26-28 SPLIMAGE files have been included in SPL files submitted to the FDA, and subsequently transmitted to DailyMed.
- Additionally, over 1430 product images have been produced from samples acquired via the C3PI project. These samples were a direct purchase of Rx products.
 - NLM is preparing SPLIMAGE specification files from these images
 - These images may be able to be offered to the sponsors/manufacturers of the products. If sponsors choose to, they can verify the images and include them in SPL files submitted to the FDA.
 - Going forward, NLM prefers to receive samples provided directly by the manufacturer, repackager, or relabeler. This methodology increases the

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control over the samples, and saves taxpayer money.

- The project is currently accepting new voluntary product submissions. The May 2011 Federal Register notice [here](#) contains contact information and mailing instructions.

A question was raised as to whether Federal Register notice limits inclusion of SPLIMAGES in PILLBOX to those photographs taken by NLM of product samples provided voluntarily by sponsors. Results from a non-binding, informal poll of workshop attendees on the potential usability of other SPLIMAGES favored the use of any SPLIMAGE, provided it was verified by a sponsor and submitted to the FDA in an SPL file. Inclusion of appropriate disclaimer text stating “which is which” would provide transparency and additional information to PILLBOX users.

Questions for further discussion:

- Would sponsors agree to receive these SPLIMAGE files for possible use in SPL files?
- Do sponsors think that they would be able to verify the SPLIMAGE against the actual product, to determine if the image was suitable for SPL inclusion?
- Would sponsors provide samples of products without SPLIMAGE files to NLM, so that SPLIMAGE files could be produced?
- Would sponsors consider taking SPLIMAGE photographs according to the SPLIMAGE specification, and then submitting them in SPL to the FDA?
- Do you, as a sponsor, have a preference as to how your SPLIMAGE files are sourced (via NLM, photographs taken by/for your company, other)?
- Do you, as a sponsor or user, believe that images used in the production version of PILLBOX should be limited to only those received by voluntary submission by sponsors and photographed by NLM sources?
- Are you supportive of the use of SPLIMAGEs obtained by a variety of means, all taken according to the SPLIMAGE specification?

Digital Photography of SPLIMAGES [\[Slideset available\]](#)

The overview of the science and technology behind the images was detailed and informative. Workshop attendees appreciated the chance to put the photography into context, and to hear rationale behind the complexities of the digital macrophotography. The slide set includes an

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equipment list, which would help sponsors or vendors determine what costs (estimated roughly as approximately \$10,000 for the equipment) would be incurred for in-house photography.

A demonstration of the tools and the process was provided later in the day. SPL Working Group representatives suggested that there be some sort of follow-up presentation or webinar to share the knowledge with a broader audience. Potential issues when setting up this type of digital macrophotography studio include:

- Lighting should be chosen and placed to prevent specular highlights (bright spots appearing on glossy tablets and capsules as a result of the light beam)
- Color calibration is critical. Some of the images from early 'pill picture' sites clearly illustrate the color variability that may be present between photography sessions or perhaps between individual lots of the product.
- Having a sample size of more than one sample of each product allowed the photographer to choose the tablet or capsule for its most representative characteristic(s). The sample size also allowed for breakage or other product marring.

Questions for further discussion:

- If one of my SPLIMAGE samples has been discontinued, or the product data elements have changed, how difficult would it be to get another SPLIMAGE? *Currently, the process follows the Federal Register notice. However, longer term, sponsors will need to consider image upkeep as part of the SPL file lifecycle.*
- Would sponsors provide samples of products without SPLIMAGE files to NLM, so that SPLIMAGE files could be produced?
- Would sponsors consider taking SPLIMAGE photographs according to the SPLIMAGE specification, and then submitting them in SPL to the FDA?
- Do you, as a sponsor, have a preference as to how your SPLIMAGE files are sourced (via NLM, photographs taken by/for your company, other)?
- Would you, or your organization, attend a class, training session or webinar to understand the details involved in compliance with the specification? Why/why not?
- If you support such a training opportunity, how would you like to see it offered? Possibilities might include
 - Provision by a trade group
 - Provision by DIA or RAPS or similar
 - Provision by NLM, FDA or a combination of both

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Early Experience with the SPLIMAGE data - Respondents to the NLM FR Notice

Representatives from three of the four pharmaceutical companies that supplied samples for image capture included individuals from Bayer, GSK, and Teva. Sponsors provided varying number of samples. All sponsors received images back from NLM in June 2012.

Some observations (from one or more of the volunteer organizations):

- The processes for gaining approval to send samples were generally positive, and did not require a high level of approval.
- Some sponsors alluded to similar activities in the past, such as those for providing samples for photography to the Physicians Desk Reference or other pictorial references.
- Sponsors provided either a few samples or their entire product line.
- Sponsors did reach out to NLM resources with questions about the sample provision and photography, and were satisfied with the additional information provided.
- Sponsors that sent less than 100% of their products were amenable to providing the remaining samples.
- The use of a file nomenclature of <NDC Number>-<non-product-characterstring>.jpg was helpful – especially when browsing through a list of files to choose the right one for the SPL being created. Sponsor representatives preferred a somewhat ‘human-readable’ file name. The use of the NDC code also connected to the product. The possibility that the image might apply to more than one NDC for the product did not impede sponsors from determining where the file belonged.
- Sponsors liked the convenience of free photography of product images, and wanted to see the option remain.
- [AREA FOR IMPROVEMENT]: Sponsors mentioned the lag time between initial submission of samples and the ultimate receipt of SPLIMAGE files or access to those files. In some cases, they contacted the email address in the Federal Register notice or people involved in the process at NLM, and got timely replies on the progress. Ideally, sponsors would like the following:
 - An e-mail or other electronic receipt or packaging list indicating that the samples were received (including a time/date of when they were received); and
 - A projected date/time period when images would be available.
- Sponsors may consider taking SPLIMAGEs inside their organization or using a vendor/outsourcer to provide them over the long-term. Reasons included the possibility of connecting the image creation to other processes that included product photography; the removal of an ‘extra step’ of obtaining/packaging/shipping samples; the increase in control over the samples (for products that may have special packaging or storage needs).

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- Sponsors were amenable to sharing their general experiences with a broader audience, such as the SPL Working Group, at time(s) in the future.

DailyMed & possible downstream uses [\[slideset available\]](#)

Staff involved with DailyMed: *Wei Ma, Chandra Kola, David Zhang*

These three people are instrumental in keeping DailyMed running. They also help to grow the functionality of the system.

Possible Uses of solid oral dose form (SODF) product images – some examples:

- enhancing medicine lists, or the creation of a list of candidates for identification of a mystery tablet/capsule found at a bedside or on the floor
- visual representation of the medical product to be taken at a specific time on a specific day (personalized medical regimens via mobile phone app) – already being explored at NLM, academic/research institutes such as MIT.
- Ensuring uniqueness of appearance (compliance with [21 CFR 206](#))
i.e, drug product in solid oral dosage form may not be introduced or delivered for introduction into interstate commerce unless it is clearly marked or imprinted with a code imprint that, in conjunction with the product's size, shape, and color, permits the unique identification of the drug product and the manufacturer or distributor of the product. [21 CFR 206.10]

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Questions and suggestions for further discussion:

- If photos are taken by someone other than NLM, how do sponsors plan to verify that an image is compliant with the published [SPLIMAGE specification](#)?
- Do sponsors think that they would be able to verify the SPLIMAGE provided by NLM against the actual product, to determine if the image was suitable for SPL inclusion?

The current validation rule on the SPLIMAGE within the FDA systems requires only that the file be in JPG/JPEG format.

- In your opinion, might additional validation rules be needed? Why?
- If so, what might those be?

Post-workshop suggestion: One attendee recommended that the current SPLIMAGE Guidelines be enhanced for manufacturers who want to submit their own photography to address additional product placement guidelines, e.g., positional placement of SODF based upon imprint information.

Using the Betapace tablets as an example, the guideline would be to place the tablet side with the product name on top (position 1) and the tablet side with the strength on the bottom (position 2). As the number of images increase, it will be important for the user to see standardized placement of information imprinted on the tablet sides – e.g., manufacturer names/logos, strength imprint, numeric imprints, blank sides, etc.

Data mining and cross-checking of metadata (controlled vocabulary fields in the Product Data Elements) against the characteristics of the SODF image has identified some records that contain inconsistencies. Going forward, DailyMed viewers may observe these inconsistencies and want to communicate them to those creating the SPL.

- Would companies find it valuable to know about these?
- How would companies prefer to be alerted? Some possibilities could be
 - via an NLM communication directly to the contact identified in the SPL
 - via an FDA communication directly to the contact identified in the SPL
 - via an FDA communication via the Review Division to the contact identified on 356h form or other formal channel
 - via an NLM communication in some broadcast or generally available form via DailyMed
 - directly from the observer?

Repackers and relabelers:

- Should they include image of product as provided by reference drug manufacturer?

Questions and suggestions for further discussion:

Authorized generics that have the same shape, size, color, imprints and physical characteristics as the reference listed drug :

- Should they include image of product as provided by reference drug manufacturer?

Representatives of downstream users:

- Would you use the images provided by the sponsors as SPLIMAGES? Why/why not?
- Would provision of a single source repository of SPLIMAGES by a trusted authority such as the NLM be likely to change your workflow for product images of SODF?
- The 150kb limit for the jpg file size may work well for display on Daily Med, but it is significantly larger than what downstream users currently produce for pharmacy customers to receive, distribute and display.
 - How might we determine if/what other sizes are needed? For instance, it may depend upon the community, clinic, or hospital pharmacy's technology and data transmission constraints.
 - Is it possible for a downstream user to resize the SPL image to a smaller file size without significant loss of quality?

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Overall Actions:

- SPL Working Group to create minutes. These will be reviewed by the attendees, revised, and disseminated. The minutes will be posted on the SPL Working Group WIKI, at minimum for view, download and further transmission.
- SPL Working Group to provide a Q&A document via WIKI for additional support. Post-meeting note: These are available [here](#).
- Slide sets presented at the workshop to be available for dissemination. Slide sets will be posted on the Working Group WIKI, at minimum.
- NLM to consider the need for a modification or amendment to the May 2011 Federal Register notice to explicitly allow SPLIMAGES taken according to the SPLIMAGE specification by entities other than NLM or its contractors.
- The vendor representatives at the workshop to initiate a discussion at an upcoming SPL Working Group Technical Team meeting about sample provision and SPLIMAGE inclusion.
- NLM to create SPLIMAGES from the other image files available as a result of CP3I purchases of samples.
- NLM, in conjunction with FDA, to identify those sponsors that have one or more products in the SPLIMAGES being rendered from the remaining C3PI collection, and to determine if/how those sponsors can obtain the SPLIMAGES.
- The sponsor representatives to share their SPLIMAGE observations and experiences so far with the broader SPL Working Group.
- Downstream user representatives to communicate their support of the inclusion of SPLIMAGE files in the SPL, and to encourage the ongoing development of a single source (such as DailyMed) for access to product images.
- NLM to further investigate the feasibility of being the host and custodian of a solid oral dose formulation image repository for access and usage by multiple stakeholders

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